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| **Development of Inhaled Therapeutic Polymeric Nanoparticles for the Treatment of Respiratory Infections** |
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| **Background:**  Respiratory diseases and infections are a considerable global public health concern. They rank third and fourth among the leading causes of death worldwide (WHO), with lower respiratory infections as the leading communicable cause of death resulting in 2.6 million deaths in 2019. Treatment of bacterial respiratory infections is becoming increasingly problematic given the rise in multi-drug resistant bacteria.  Nitric oxide (NO) is a promising antimicrobial and an alternative to antibiotics. NO has been shown to effectively kill a broad range of bacteria, viruses and fungi due to its ability to disrupt the cellular functions of such microorganisms. Given its multimechanistic mode of action, there is little tendency for bacteria to develop resistance mechanisms. However as NO is a gas, delivery to the site of an infection is challenging.  Nanoparticles have a well-established use in pharmaceuticals, with their small size allowing for targeted delivery and increased bioavailability. Hyperbranched polymeric nanoparticles, have proven to be an effective drug delivery vehicles and have demonstrated good applicability for inhaled applications. The aim of this project is to develop hyperbranched polymeric drug delivery vehicles that will encapsulate nitric oxide donors for inhaled drug delivery applications. |
| **Methods:**  Both the linear and hyperbranched forms of an hyperbranced polymer were synthesised in anaerobic conditions. These polymers were modified and nitrosylated to form NO-donating compounds. NO release was directly measured in PBS under varying conditions (light/ dark, EDTA) by chemiluminescence. |
| **Results:**  Structural analysis of the synthesised hyperbranched polymers was characterised using Fourier-transform infrared spectroscopy (FTIR), 1H, 13C, COSY, HSQC, HMBC, 13C DEPT-135 nuclear magnetic resonance spectroscopy (NMR), gel permeation chromatography (GPC). |
| **Conclusions:**  We have synthesised linear and hyperbranched polymeric drug delivery carriers and nitrosylated them to form stable NO donating compounds, which show a sustained release of NO. Ongoing and future work includes the optimisation of the chain length and microbiology testing. |